

WHAT IS CLAIMED IS:

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1. A method for lowering blood glucose levels in human patients needing treatment for non-insulin-dependent diabetes mellitus (NIDDM), comprising orally administering to human patients on a once-a-day basis at least one oral controlled release dosage form comprising an effective dose of at least one suitable antihyperglycemic agent or a pharmaceutically acceptable salt thereof and a controlled release carrier, wherein the dosage form provides a mean time to maximum plasma concentration ( $T_{max}$ ) of metformin at from 5.5 to 7.5 hours after administration.

Note: renally impaired indiv. have delay  $T_{max}$

2. The controlled release dosage form of claim 1 wherein said at least one antihyperglycemic agent is a biguanide.
3. The controlled release dosage form of claim 2 wherein said biguanide is metformin or a pharmaceutically acceptable salt thereof.

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4. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean time to maximum plasma concentration ( $T_{max}$ ) of metformin at from 6.0 to 7.0 hours after administration.

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5. The method of claim 3, in which the administration of the at least one metformin dosage form occurs at dinner time and provides a mean time to maximum plasma concentration ( $T_{max}$ ) of metformin at from about 5.5 to 7.0 hours after the administration.

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6. The method of claim 3, in which the administration of the at least one metformin dosage form occurs at breakfast and provides a mean time to maximum plasma concentration ( $T_{max}$ ) of metformin at from about 6.0 to about 7.5 hours after the administration.

7. The method of claim 3, in which the administration of the at least one metformin dosage form provides a width at 50% of the height of a mean plasma concentration/time curve of the drug from about 4.5 to about 13 hours.
8. The method of claim 3, in which the administration of the at least one metformin dosage form provides a width at 50% of the height of a mean plasma concentration/time curve of the drug from about 5.5 to about 10 hours.
9. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean maximum plasma concentration ( $C_{max}$ ) of metformin which is more than about 7 times the mean plasma level of said metformin at about 24 hours after administration.
10. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean maximum plasma concentration ( $C_{max}$ ) of metformin which is from about 7 times to about 14 times the plasma level of said metformin at about 24 hours after administration.
11. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean maximum plasma concentration ( $C_{max}$ ) of metformin which is from about 8 times to about 12 times the plasma level of said metformin at about 24 hours after administration.
12. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean maximum plasma concentration ( $C_{max}$ ) of metformin from about 1500 ng/ml to about 3000 ng/ml, based on administration of a 2000 mg once-a-day dose of metformin.

13. The method of claim 3; in which the administration of the at least one metformin dosage form provides a mean maximum plasma concentration ( $C_{max}$ ) of metformin from about 1700 ng/ml to about 2000 ng/ml, based on administration of a 2000 mg once-a-day dose of metformin.

14. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean  $AUC_{0-24hr}$  *to what?* from at least 80% of the mean  $AUC_{0-24}$  provided by administration of an immediate release reference standard twice a day, wherein the daily dose of the reference standard is substantially equal to the once-a-day dose of metformin administered in the controlled release oral dosage form.

15. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean  $AUC_{0-24hr}$  that is from at least 90% of the mean  $AUC_{0-24}$  provided by administration of an immediate release reference standard twice a day, wherein the daily dose of the reference standard is substantially equal to the once-a-day dose of metformin administered in the controlled release oral dosage form.

16. The method of claim 3, in which the once-a-day dose of the metformin is administered at dinner.

17. The method of claim 16, in which the once-a-day dose of metformin is administered at fed state.

18. The method of claim 16, in which the once-a-day dose of the metformin is about 2000 mg, which is provided by two controlled release dosage forms containing about 1000 mg metformin each.

19. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean  $AUC_{0-24hr}$  from about 17200 ng.hr/ml to about 33900 ng.hr/ml, based on administration of a 2000 mg once-a-day dose of metformin.
20. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean  $AUC_{0-24hr}$  from about 17200 ng.hr/ml to about 26500 ng.hr/ml, based on administration of a 2000 mg once-a-day dose of metformin.
21. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean  $AUC_{0-24hr}$  from about 19800 ng.hr/ml to about 33900 ng.hr/ml, based on administration of a 2000 mg once-a-day dose of metformin.
22. *omnibus* The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean plasma concentration-time profile of metformin substantially as set forth in FIG. 1, based on administration of a 1700 mg once-a-day dose of metformin.
23. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean plasma concentration-time profile of metformin substantially as set forth in FIG. 2, based on administration of a 2000 mg once-a-day dose of metformin.
24. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean plasma concentration-time profile of metformin substantially as set forth in FIG. 4, based on administration of a 2000 mg once-a-day dose of metformin at dinner.
25. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean plasma concentration-time profile of metformin substantially as set

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Cont. forth in FIG. 6, based on administration of a 2000 mg once-a-day dose of metformin at breakfast.

26. The method of claim 3, in which the administration of the at least one metformin dosage form provides a mean plasma glucose concentration-time profile substantially as set forth in FIG. 5, based on administration of a 2000 mg once-a-day dose of metformin at dinner.

27. The method of claim 3, further comprising administering to said human patients at least one additional pharmaceutically active ingredient for treatment of NIDDM.

28. The method of claim 3, further comprising administering to said human patients an additional pharmaceutically active ingredient for treatment of NIDDM, said additional pharmaceutically active ingredient selected from the group consisting of a sulfonylurea, a glitazone or a second biguanide.

29. The method of claim 3, in which the dose of metformin comprises metformin hydrochloride.

30. The method of claim 29, in which the once-a-day dose of metformin hydrochloride is about 1000 mg to about 2500 mg.

31. The method of claim 29, in which the once-a-day dose of metformin hydrochloride is about 2000 mg to about 2500 mg metformin.

32. A method for lowering blood glucose levels in human patients needing treatment for non-insulin-dependent diabetes mellitus (NIDDM), comprising orally administering at least one biguanide or pharmaceutically acceptable salt thereof and a controlled release carrier wherein a single administration of said dosage form provides a higher mean fluctuation

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